Insulin resistance plays a pathogenic role in type 2 diabetes, hypertension, and cardiovascular disease (1). Insulin resistance may precede atherosclerosis by variable lengths of time, and type 2 diabetes by as many as 10 y (2). Insulin resistance can be defined as a diminished ability of the cell to respond to the action of insulin, and is usually compensated by hyperinsulinemia. Different cytokines synthesized by adipocytes, macrophages, or lymphocytes may influence the development of insulin resistance, including leptin, adiponectin, resistin, retinol binding protein-4 (RBP-4), tumor necrosis factor-α (TNF-α), and interleukin-6 (IL-6) (3). Some of these cytokines, such as TNF-α, activate a number of protein kinases that target elements along the insulin signaling pathway. For instance, some kinases induce the autophosphorylation of the insulin receptor (IR), and then phosphorylate the insulin receptor substrate-1 (IRS-1). IRS-1 tyrosine phosphorylation promotes the transcriptional and mitogenic activity of insulin, and stimulates the translocation of glucose transporter 4 (GLUT4) to the cell membrane. The default of this signal transduction could lead to the development of insulin resistance (4).

Although both genetic and environmental factors can contribute to the development of insulin resistance, dietary patterns have been suggested as being a crucial factor (5). Several studies focusing specifically on glycemic index (GI) showed that a low-GI diet can improve insulin sensitivity (6–8). In 1981 Jenkins et al. (9) first introduced the concept of GI, defined as the incremental area under the blood glucose response curve following ingestion of a 50 or 25 g carbohydrate portion of a test food. Specifically, the GI is expressed as a percentage of the response to the same amount of carbohydrates from a standard food taken by the same subject for a 2 h period.

Plant-based starchy foods are the main carbohydrate sources worldwide. Choosing a higher quality of carbohydrates is important for preventing and managing insulin resistance or type-2 diabetes. Higher or lower-GI starches can produce different postprandial

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**Sweet Potato [Ipomoea batatas (L.) Lam. “Tainong 57”] Starch Improves Insulin Sensitivity in High-Fructose Diet-Fed Rats by Ameliorating Adipocytokine Levels, Pro-Inflammatory Status, and Insulin Signaling**

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**Summary** The aim of this study was to investigate the effects of low-glycemic index (GI) sweet potato starch on adipocytokines, pro-inflammatory status, and insulin signaling in the high-fructose diet-induced insulin-resistant rat. We randomly divided 24 insulin-resistant rats and 16 normal rats into two groups fed a diet containing 575 g/kg of starch: a low-GI sweet potato starch (S) or a high-GI potato starch (P). The four experimental groups were labeled as follows: insulin-resistant P (IR-P), insulin-resistant S (IR-S), normal P (N-P) and normal S (N-S). After 4 wk on the experimental diets, an intraperitoneal glucose tolerance test (IPGTT) was conducted, and the homeostasis model assessment (HOMA), adipocytokines, pro-inflammatory cytokines levels, and insulin signaling-related protein expression were measured. The homeostasis model assessment values were significantly lower in the IR-S than in the IR-P group, suggesting that insulin sensitivity was improved among sweet potato starch-fed rats. Levels of tumor necrosis factor-α, interleukin-6, resistin, and retinol binding protein-4 were significantly lower in the IR-S versus the IR-P group, indicating an improvement of pro-inflammatory status in sweet potato starch-fed rats. The sweet potato starch diet also significantly enhanced the protein expression of phospho-Tyr-insulin receptor substrate-1 and improved the translocation of glucose transporter 4 in the skeletal muscle. Our results illustrated that sweet potato starch feeding for 4 wk can improve insulin sensitivity in insulin-resistant rats, possibly by improving the adipocytokine levels, pro-inflammatory status, and insulin signaling.

**Key Words** sweet potato, glycemic index, insulin sensitivity, inflammatory cytokines, insulin signaling

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insulin responses and may affect the insulin sensitivity. For instance, our laboratory previously established the GI value of sweet potato (Tainong 57) to be 55.0±6.6 (10), which places it in the low-GI food category. In addition, the rich content of dietary fiber (2.4 g/100 g) (11) as well as high amounts of vitamin A and C makes the sweet potato a popular healthy starch that is being used as a substitute for rice by many Asians. Some studies reported that a high-fructose diet can result in an increased secretion of TNF-α and diminished adiponectin levels. This pro-inflammatory state is likely to result in whole-body pathologies, including insulin resistance (12–14). In fact, a clear association between pro-inflammatory signaling and decreased insulin sensitivity has been revealed (15). Several mechanisms may be responsible for the effects of dietary GI on insulin sensitivity (16, 17). However, the effect of dietary GI on insulin signaling and adipocytokines or pro-inflammatory cytokines remains unclear. It is hypothesized that the low-GI sweet potato starch positively affects insulin sensitivity via the regulation of adipocytokines, pro-inflammatory cytokines concentrations and insulin signaling. The aim of this study was to investigate the effects of sweet potato starch feeding on insulin signaling in the high-fructose diet-induced insulin-resistant rat model. In addition, we also attempted to determine whether sweet potato starch affects insulin sensitivity via the regulation of adipocytokines or pro-inflammatory cytokine concentrations.

MATERIALS AND METHODS

High-fructose diet-induced insulin-resistant animals. Male Sprague-Dawley rats (n=40, aged 8 wk) were obtained from BioLASCO Taiwan (Taipei, Taiwan). Taipei Medical University approved the use of these laboratory animals while the experimental plan was approved by the Institutional Animal Care and Use Committee of Taipei Medical University (LAC-99-0309). Following a 1-wk adaptation, the rats were divided into two groups. In order to induce insulin resistance, the first group of rats (n=24) was randomly assigned to receive a fructose-rich chow diet containing 60% fructose, 5% fat and 18% protein (Harlan Teklad, Madison, WI; Cat. Number TD 89247) for 6 wk (18). The control group (n=16) received a standard chow diet during the same 6-wk period. At the end of 6 wk, the homeostasis model assessment of basal insulin resistance (HOMA) was used to quantify insulin resistance. HOMA was calculated as the product of the fasting concentrations of plasma glucose (mmol/L) and plasma insulin (μU/mL) divided by 22.5 (19). Lower HOMA values indicated greater insulin sensitivity.

At the end of 6 wk, the levels of blood glucose, insulin and HOMA values increased significantly in fructose-fed rats compared to the chow diet-fed rats (Table 1). These results indicate the development of insulin resistance and hyperinsulinemia in rats on the 6-wk high-fructose diet.

Establishing the GI of the experimental starches. Our laboratory previously established that the mean±standard error of the mean (SE) GI value of sweet potato (Tainong 57) was 55.0±6.6 while the GI value of potato was 85.4±4.7. In this study, we used sweet potato as the source of low-GI starch, and potato as the source of high-GI starch. The cooked 100% sweet potato starch was obtained from Abundant States Starch Manufacturing Factory (Chiayi County, Taiwan, produced from Tainong no. 57 sweet potato), and the cooked 98% potato starch was obtained from Kuo Chi Trading Co. (Taipei, Taiwan, produced from Kennebec potato). To verify the GI values of these commercial starches, we measured their GI values according to the GI testing protocol (20) using 50 mL of a 50% glucose solution (25 g glucose) as the reference food. We enrolled 13 healthy people with a mean age of 22.1 y. The study was approved by the Institutional Review Board of Taipei Medical University, and written informed consent was obtained from every subject. On each test day, over a period of 15 min, all subjects consumed a starch containing 25 g of carbohydrates. Venous blood was sampled in a heparin-containing tube at 0 (initiation of ingestion), 30, 45, 60, 90, and 120 min after ingestion. Blood samples were centrifuged (1,400 ×g for 10 min at 4˚C) to obtain plasma. Blood sugar was measured with a commercial kit (Glucose Oxidase and Peroxidase, Randox Lab, Co., Antrim, UK).

To calculate GI values, the area under the curve (AUC) of glucose levels must be identified in advance. As previously described (9), the GI of the commercial starches was identified as the area under the glycemic curve of the starches or the area under the glycemic curve of glucose. This investigation revealed that the mean±SE GI of commercial sweet potato starch and potato starch was 52.2±3.7 and 91.0±10.6 respectively. Accordingly, sweet potato starch belonged to the low-GI category, while potato starch belonged to the high-GI category. This demonstrates that the two types of starches are suitable for use as low and high-GI sources for our study.

Treatment protocol. The 24 insulin-resistant rats and 16 normal rats were randomly assigned to a diet containing 575 g/kg (21) of cooked 100% sweet potato starch (S) or cooked 98% potato starch (P). The com-

| Table 1. Levels of blood glucose, insulin, and HOMA values in rats following 6 wk of a high-fructose diet. |
|---------------------------------|-------------------|-------------------|
|                                 | Chow diet-fed rats | High-fructose diet-fed rats |
|                                 | (n=16)            | (n=24)            |
| Body weight (g)                 | 412.9±2.7         | 414.5±1.3         |
| Fasting glucose (mg/dL)         | 110.0±1.8         | 135.8±1.2*        |
| Insulin (μU/mL)                 | 61.4±1.6          | 85.0±0.8*         |
| HOMA values                     | 16.7±0.5          | 28.4±0.3*         |

Data are presented as mean±SE.

Statistical analysis was performed using the unpaired t-test.

*p<0.05.
position of the experimental diets is listed in Table 2. The four experimental groups were labeled as follows: insulin-resistant P (IR-P), insulin-resistant S (IR-S), normal P (N-P) and normal S (N-S). Blood samples were obtained from the tail vein and collected in EDTA-containing tubes prior to feeding and following an overnight fast. Levels of leptin, adiponectin, resistin, RBP-4, TNF-α, and IL-6 were measured in the blood to establish the baseline. Following 4 wk on these diets, the rats underwent an intraperitoneal glucose tolerance test (IPGTT) to evaluate the effect of the low-GI sweet potato starch on insulin sensitivity. The rats fasted overnight and the blood samples were taken from the tail vein (time 0). A glucose challenge was given intraperitoneally (2 g glucose/kg body weight) and subsequent blood samples were taken at 15, 30, 60, 90, 120, 150, and 180 min. The plasma glucose concentrations were determined spectrophotometrically using a glucose kit (Randox). The plasma insulin level was measured by a Rat Insulin ELISA kit (Merckodia, Uppsala, Sweden). The AUC for blood glucose and insulin was also calculated. Blood glucose and insulin levels at time 0 were used to calculate the HOMA values.

At the end of the 4 wk, the rats were fasted overnight and the blood samples were obtained from the tail vein and collected in EDTA-containing tubes for further lipid, leptin, adiponectin, resistin, RBP-4, TNF-α and IL-6 measurements. Then the rats underwent insulin stimulation under a fasting condition. Insulin stimulation was performed with intraperitoneal injection of 15 U/kg regular insulin. After waiting 30 min following injection for the effect of insulin to occur (22, 23), the rats were anesthetized with Rompun and Zoletil. Each animal’s gastrocnemius muscle was removed, weighed, frozen in liquid nitrogen, and subsequently stored at −80°C for protein expression studies.

Measurement of lipid, adipocytokine, and pro-inflammatory cytokine concentrations. Plasma triglycerides, total cholesterol, high- and low-density lipoprotein cholesterol (HDL-C and LDL-C, respectively), and non-esterified fatty acid (NEFA) concentrations were determined spectrophotometrically using a triglycerides kit, cholesterol kit, LDL-C kit and NEFA kit, respectively (Randox). Adiponectin was measured by an AssayMax Rat Adiponectin ELISA kit (Assaypro, St. Charles, MO), while resistin and leptin were measured by a Rat Resistin and Leptin ELISA kit (BioVendor, Brno, Czech Republic). RBP-4 was measured by a Rat Retinol BP ELISA kit (ICL, Portland, OR). TNF-α and IL-6 were measured by a Rat TNF-α and IL-6 Platinum ELISA Kit (eBioscience, Vienna, Austria).

Western blotting. Skeletal muscles were homogenized in Pro-PrepTM protein extraction solution (iNtRON Biotechnology, Gyeonggi-do, Korea) with a polytron (Brinkmann Instruments, Westbury, NY) for assaying with phopho-Tyr-IR and phopho-Tyr-IRS-1. The plasma membrane extraction of skeletal muscle for the GLUT4 translocation assay was prepared by using a plasma membrane protein extraction kit (BioVision, Milpitas, CA, Cat. Number: K268-50) according to the manufacturer’s instructions. Skeletal muscle plasma membrane was re-suspended in 0.5% Triton X-100 in phosphate-buffered saline before use. Protein concentrations in each sample were quantified using a commercial assay kit (Bio-Rad DC Protein Assay kit, Bio-Rad Laboratories, Hercules, CA) with bovine serum albumin (BSA) serving as a standard. Equal amounts of protein (30 μg) were denatured and separated by 10% sodium dodecylsulfate polyacrylamide gel electrophoresis (SDS-PAGE). After separation, the proteins were electroblotted onto a polyvinylidene difluoride transfer membrane (Amer sham Biosciences, Little Chalfont, UK). These blots were then incubated with anti-phospho-Tyr-IR (Millipore, Billerca, MA), anti-phospho-Tyr-IRS-1 (Millipore), and anti-GLUT4 (Millipore). Finally, the blot was treated with goat anti-mouse immunoglobulin G horseradish peroxidase (IgG-HRP; Millipore) or goat anti-rabbit IgG-

Table 2. Composition of diets used in this study.

<table>
<thead>
<tr>
<th>Component</th>
<th>Amount (g/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sweet potato starch or potato starch</td>
<td>575</td>
</tr>
<tr>
<td>Vegetable and animal fat1</td>
<td>55</td>
</tr>
<tr>
<td>Casein</td>
<td>230</td>
</tr>
<tr>
<td>Mineral mix2</td>
<td>70</td>
</tr>
<tr>
<td>Vitamin mix2</td>
<td>10</td>
</tr>
<tr>
<td>Cellulose</td>
<td>60</td>
</tr>
</tbody>
</table>

1 In g/kg of the diet: corn oil 13, peanut oil 14, and lard 28.
2 Based on the American Institute of Nutrition-93 diet composition.

Table 3. Characteristics of rats following 4 wk of a diet containing 575 g/kg of sweet potato or potato starch.

<table>
<thead>
<tr>
<th></th>
<th>N-P (n=8)</th>
<th>N-S (n=8)</th>
<th>IR-P (n=12)</th>
<th>IR-S (n=12)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial BW (g)</td>
<td>411.4±4.5</td>
<td>414.4±3.3</td>
<td>416.8±1.8</td>
<td>412.3±1.9</td>
</tr>
<tr>
<td>Final BW (g)</td>
<td>544.6±7.6b</td>
<td>559.8±5.4a</td>
<td>518.0±5.5a</td>
<td>530.3±8.6ab</td>
</tr>
<tr>
<td>BW gain (g)</td>
<td>137.9±8.9b</td>
<td>145.7±7.2b</td>
<td>97.0±4.0a</td>
<td>120.6±8.1ab</td>
</tr>
<tr>
<td>Feeding efficiency (%)</td>
<td>18.9±1.3b</td>
<td>20.1±0.9b</td>
<td>12.9±0.5a</td>
<td>16.2±1.1ab</td>
</tr>
<tr>
<td>Liver weight (g)</td>
<td>12.3±0.3ab</td>
<td>13.5±0.9b</td>
<td>11.2±0.3a</td>
<td>12.9±0.4b</td>
</tr>
</tbody>
</table>

Data are presented as mean±SE.
Means with a different superscript differ significantly (p<0.05) according to the two-way ANOVA with the Tukey-Kramer test.
Sweet Potato Starch Improves Insulin Signaling

HRP (Santa Cruz Biotechnology, Santa Cruz, CA), and specific bindings of antibodies were detected using an enhanced chemiluminescence Western blot detection kit (Thermo Scientific, Rockford, IL). The bands were quantified using Image-Pro Plus 4.5 software.

Statistical analysis. All data are presented as the mean±SE. Unpaired $t$-tests were used to compare the data between chow- and fructose-fed rats after high-fructose diet feeding for 6 wk. Paired $t$-tests were used to compare the data between baseline and after 4-wk feeding in the same group. A two-way analysis of variance (ANOVA) with a Tukey-Kramer test was used to compare the four groups following 4 wk of experimental diet feeding. All statistical analyses were performed

<table>
<thead>
<tr>
<th></th>
<th>N-P ($n=8$)</th>
<th>N-S ($n=8$)</th>
<th>IR-P ($n=12$)</th>
<th>IR-S ($n=12$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting glucose (mg/dL)</td>
<td>114.1±3.0$^a$</td>
<td>111.9±2.7$^a$</td>
<td>135.6±1.6$^b$</td>
<td>130.4±2.0$^b$</td>
</tr>
<tr>
<td>Insulin (µU/mL)</td>
<td>62.7±1.7$^a$</td>
<td>61.0±1.6$^a$</td>
<td>88.7±1.1$^c$</td>
<td>75.3±0.8$^b$</td>
</tr>
<tr>
<td>HOMA values</td>
<td>17.7±0.7$^a$</td>
<td>16.9±0.8$^a$</td>
<td>29.7±0.4$^c$</td>
<td>24.2±0.4$^b$</td>
</tr>
<tr>
<td>Cholesterol (mg/dL)</td>
<td>52.6±6.3</td>
<td>47.3±4.3</td>
<td>53.9±5.1</td>
<td>51.4±4.0</td>
</tr>
<tr>
<td>Triglycerides (mg/dL)</td>
<td>58.8±3.5$^a$</td>
<td>63.3±7.3$^a$</td>
<td>82.8±4.6$^b$</td>
<td>84.1±3.9$^b$</td>
</tr>
<tr>
<td>HDL-C (mg/dL)</td>
<td>21.3±1.0$^b$</td>
<td>20.4±1.2$^b$</td>
<td>17.4±0.7$^a$</td>
<td>17.1±0.8$^a$</td>
</tr>
<tr>
<td>LDL-C (mg/dL)</td>
<td>5.8±0.7$^bc$</td>
<td>3.9±0.4$^a$</td>
<td>6.0±0.5$^c$</td>
<td>4.5±0.4$^{ab}$</td>
</tr>
<tr>
<td>NEFA (mmol/L)</td>
<td>0.6±0.04$^a$</td>
<td>0.6±0.03$^a$</td>
<td>1.2±0.06$^b$</td>
<td>1.1±0.06$^b$</td>
</tr>
</tbody>
</table>

Data are presented as mean±SE. Means with a different superscript differ significantly ($p<0.05$) according to the two-way ANOVA with the Tukey-Kramer test.

Fig. 1. (a) The curve, (b) AUC of blood glucose during the IPGTT following 4 wk of a diet containing 575 g/kg of sweet potato or potato starch. Data are presented as mean±SE. Means with a different superscript differ significantly ($p<0.05$) according to the two-way ANOVA with the Tukey-Kramer test.

Fig. 2. (a) The curve, (b) AUC of blood insulin during the IPGTT following 4 wk of a diet containing 575 g/kg of sweet potato or potato starch. Data are presented as mean±SE. Means with a different superscript differ significantly ($p<0.05$) according to the two-way ANOVA with the Tukey-Kramer test.
using Statistical Analytic System 8.0 (SAS Institute Inc., Cary, NC). Differences between groups were considered statistically significant if $p$-values were less than 0.05.

**RESULTS**

**Effect of sweet potato starch feeding for 4 wk on insulin sensitivity**

Tables 3 and 4 outline the characteristics and blood parameter levels of all rats after 4 wk of consuming the high and low-GI experimental diets. Mean levels of fasting blood glucose, insulin, triglycerides, NEFA, and HOMA values were significantly higher among insulin-resistant rats than among control rats. Additionally, insulin level and HOMA values were significantly lower in the IR-S versus the IR-P group. These results show that a diet comprising sweet potato starch improves hyperinsulinemia and insulin sensitivity in insulin-resistant rats in comparison to a diet of high-GI potato starch.

In comparison to control rats, insulin-resistant rats also had a higher blood glucose and insulin AUC (Figs. 1 and 2, respectively). This indicated the presence of glucose intolerance and insulin resistance in insulin-resistant rats. Additionally, our results show that both the glucose and insulin AUC was obviously greater in the IR-P group than in the IR-S group. This result demonstrates that a diet of low-GI sweet potato starch improves the postprandial blood glucose response and increases the glucose and insulin tolerance of insulin-resistant rats, by contrast to the high-GI potato starch diet.
Effect of a 4-wk sweet potato starch diet on adipocytokine and pro-inflammatory cytokine levels

Levels of adipocytokines and pro-inflammatory cytokines are listed in Table 5. Briefly, baseline levels of leptin, resistin, RBP-4, TNF-α, and IL-6 were significantly higher in insulin-resistant rats than in normal rats. After 4-wk feeding on the experimental diets, levels of leptin, resistin, IL-6, TNF-α, and RBP-4 were significantly higher in the insulin-resistant rats versus the control rats. There were no significant differences in the concentrations of adiponectin or leptin between IR-P and IR-S groups. However, the concentrations of resistin, RBP-4, IL-6, and TNF-α were significantly lower in the IR-S group in comparison to the IR-P group. In other words, a low-GI diet comprising sweet potato could reduce the blood concentrations of certain adipocytokines and pro-inflammatory cytokines.

Effect of 4-wk sweet potato starch diet on protein expression related to insulin signaling

Figures 3–5 illustrate the expression of muscle proteins related to insulin signaling, including phospho-Tyr-IR, phospho-Tyr-IRS-1 and GLUT4. A high-fructose diet and the sweet potato starch intervention diet had no significant effect on the protein expression of
phospho-Tyr-IR. However, the protein expressions of phospho-Tyr-IRS-1 were significantly lower in the insulin-resistant rats than in the control rats. Thus, the high-fructose diet decreased the expression of phospho-Tyr-IRS-1. Four weeks of sweet potato starch feeding produced a significant increase of phospho-Tyr-IRS-1 expression compared to potato starch feeding. In addition, the protein expression of GLUT4 in the plasma membrane was significantly higher in IR-S group than in the IR-P group. Accordingly, our findings demonstrate that a sweet potato starch diet improved insulin signaling and the insulin-stimulated translocation of GLUT4.

**DISCUSSION**

In the present study, we found that a diet of low-GI sweet potato starch improves insulin sensitivity in high-fructose diet-induced insulin-resistant rats and is associated with an improvement in adipocytekine levels, pro-inflammatory status, and insulin signaling. Overproduction of pro-inflammatory cytokines and certain adipokynes is closely associated with insulin resistance (24). Ahima and Lazar (25) suggested that high blood levels of resistin and IL-6 could induce insulin resistance in rodents. Similarly, infusion of TNF-α in rodents leads to impairment of insulin-stimulated skeletal muscle glucose uptake (26). Finally, blood RBP-4 levels are elevated in several mouse models of insulin resistance, and the deletion of the RBP-4 gene in mice has been shown to increase insulin sensitivity (27). Accordingly, levels of resistin, IL-6, TNF-α, and RBP-4 are strongly related to the development of insulin resistance. In this study, we found that a high-fructose diet induced a significant elevation in blood TNF-α and IL-6 levels. Therefore, we hypothesized that rats fed a high-fructose diet for 6 wk would develop a pro-inflammatory state. However, 4 wk of a low-GI sweet potato starch diet effectively suppressed concentrations of resistin, IL-6, TNF-α, and RBP-4 in insulin-resistant rats. These findings were closely associated with the amelioration of insulin sensitivity and glucose tolerance among rats on the sweet potato starch diet.

One possible mechanism by which sweet potato starch decreases the production of pro-inflammatory cytokines may involve nuclear factor-κB (NF-κB). Motton et al. (28) demonstrated that dietary patterns that rapidly increase blood glucose and insulin concentrations postprandially (i.e., high GI) induce an inflammatory response due to the acute excess of cellular glucose. Ghanim et al. (29) mentioned that the blood mononuclear cells to use excess glucose not only for glycolysis, but also for production nicotinamide adenine dinucleotide phosphate (NADPH). NADPH will result in the generation of reactive oxygen species, and activation of the NF-κB pathway (30). NF-κB is an important factor of pro-inflammatory gene transcription. Specifically, when NF-κB is activated, it translocates to the nucleus, and acts on genes that regulate pro-inflammatory cytokines (31). In Dickinson’s study (32), the concentration of NF-κB in intranuclear mononuclear cell extracts was measured in response to 50 g glucose loads, white bread (high-GI), and pasta (low-GI). They found that the high-GI white bread meal resulted in a three-fold greater NF-κB AUC in comparison to that produced by the low-GI pasta meal. In addition, they found a significant positive relationship between NF-κB concentrations in peripheral blood mononuclear cells and fasting insulin, and observed that fasting insulin levels predicted NF-κB AUC. Therefore, we hypothesize that low-GI sweet potato starch may influence the activation of NF-κB via the moderation of insulin secretion, thereby further decreasing the production of pro-inflammatory cytokines.

Defects in insulin signaling lead to impaired glucose utilization and are believed to be an important factor in the pathogenesis of insulin resistance (33). A chronic high-fructose diet impairs insulin action by reducing the expression of insulin-stimulated protein such as IRS, IRS-1, and GLUT4 (34). In this study, we found that 6 wk of a high-fructose diet decreased the expression of phospho-Tyr-IRS-1 protein. Previous studies indicated that TNF-α inhibits insulin signaling by affecting IRS-1, including a proteosome-mediated degradation and phosphatase-mediated dephosphorylation (35, 36). Thus, a higher level of TNF-α in high-fructose diet-fed rats may explain the decreased expression of phospho-Tyr-IRS-1 in this study. Such a change could interfere with insulin action, leading to the development of insulin resistance. We also found that 4 wk of a diet comprising sweet potato starch, in comparison to a diet of potato starch, upregulated the phosphorylation of IRS-1 in the skeletal muscle of the insulin-resistant rats. Our data suggest that sweet potato starch improves insulin signaling and may play an important role in glucose metabolism or utilization. This may explain the observed improvement of insulin sensitivity among sweet potato-fed insulin-resistant rats.

Ishiki and Klip (37) suggest that glucose uptake via GLUT4 translocation is an important action of insulin and that this action is impaired in type-2 diabetes. Insulin resistance is associated with decreasing glucose uptake and utilization, as well as a reduced GLUT4 gene expression (38). The results of the current study illustrate that the GLUT4 protein in the plasma membrane of skeletal muscle was increased in sweet potato starch-fed insulin-resistant rats. We believe that sweet potato starch leads to the phosphorylation of IRS-1 and thus an improvement in insulin signaling. Finally, it induces GLUT4 to translocate to the plasma membrane and enhances glucose tolerance. Insulin action and insulin sensitivity in a fructose-induced insulin-resistant state.

This study has a few limitations that warrant discussion. First, insulin sensitivity was assessed by the HOMA method and the AUC for glucose and insulin during the IPGTT. The blood glucose or insulin AUC following glucose loading has been widely used as a simple assessment of insulin sensitivity in animals (39). However, since the intravenous glucose tolerance test developed by Finegood et al. correlates strongly with euglycemic clamp measurements of insulin sensitivity, this measure could be another standard indicator of insulin sensitivity (40).
Second, although we induced insulin resistance through 6 wk of a high-fructose diet, our rats failed to become clearly obese. However, in similar study (12), Schaalann induced insulin resistance in rats using high-fructose diet for 8 wk, and found a significant elevation in ratios of epididymal fat, visceral fat, and liver weight. Thus, the increased adipocytokine and pro-inflammatory cytokine levels measured in this study could also be produced by adipocytes. Indeed, adiponectin is believed to be produced almost exclusively by mature adipocytes. Another longer duration study of high-fructose or a high-fat diet-induced insulin-resistant and obese animal model is required to assess this potential mechanism. Third, Sridhar et al. (23) reported that insulin regulates glucose homeostasis mainly by increasing the transport of glucose into the skeletal muscle. DeFronzo et al. (41) state that skeletal muscle is the main site responsible for insulin-stimulated glucose disposal in the body. Finally, Nishiumi et al. (42) also found that muscle is the tissue consuming the greatest amount of glucose. Accordingly, we measured expression of proteins involved in insulin signaling in the skeletal muscle. However, two previous studies also demonstrated that the insulin signaling in adipocytes (43) and liver (44) would affect the insulin sensitivity and glucose tolerance. Thus, a study of insulin signaling in adipose tissue or the liver is also required.

In conclusion, the present study illustrated that the improvement in insulin sensitivity in response to a low-GI sweet potato starch diet may be due to positive changes in adipocytokine levels and pro-inflammatory status and insulin signaling in high-fructose diet-induced insulin-resistant rats.

Acknowledgments
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The authors declare no conflict of interest.

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